

REMARKS

Applicant's attorney apologizes for any confusion caused by the heading "Appendix" on the paper submitted with the previous response, it was not intended to add this to the specification, simply to provide the information set out therein to the examiner. As suggested, that information is resubmitted herewith in the form of a declaration.

A verified translation of CN 1273114 is being prepared and will be submitted as soon as possible.

Applicants have previously argued that the invention as claimed in claims 18 and 2-12, is not prima facie obvious over a combination of Gai et al Chinese Publication CN 1,273,114 and Su US Patent 4,968,675. Those arguments are maintained and reiterated below. It is additionally submitted that, as shown by the attached declaration,. The invention as claimed, which requires pH adjustment to 6.0 produces a composition having surprising stability that could not be predicted from the prior art which fact establishes patentability even if there were a prima facie case of obviousness, which is denied. The declaration clearly shows that the compositions set out in Table 2 have substantially improved stability over time as compared with those set out in Table 1. The difference between these compositions is the starting pH.

Having regard to the question of whether there is even a prima facie case to answer, it is pointed out that although Gai teaches production of an injectable composition from a saponin-containing powder obtained from notoginseng by "mixing it with injection water, regulating pH value, boiling the solution adding activated carbon, filtering and fine-filtering". Su teaches production of an injectable amino-steroid drug by dissolving the active compound in a citric acid solution and then stirring in sodium citrate and sodium chloride. The product is then filtered.

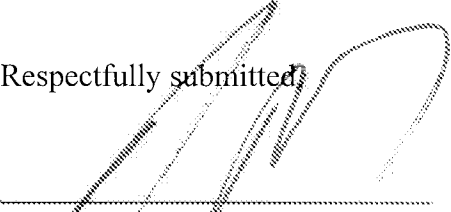
The examiner comments that the previous response did not address the fact that the examiner relied on a combination of these references and attacked them individually. It is respectfully submitted that this is not so. It was pointed out that Su does not relate to compositions containing an active component of the type specified in the present claims and so there was no basis for combining it with Gai. As pointed out previously, Su's compounds are nitrogen-containing. The compounds of the present composition are not. It is well known that the lone pair of electrons on the nitrogen atom affects the properties of compounds containing nitrogen and in particular their degree of polarity, a factor that is of importance when considering the appropriate pH of a composition in which they are to be contained. The examiner refers to *Ex parte Bland* for support for the proposition that the compounds are sufficiently similar that inferences can be drawn from them. It is submitted that this reliance is misplaced. It seems that in *Bland*, the difference between the claimed invention and the prior art was in the nature of the carrier and reasons were given as to why the carrier specified in the claims might have been expected to be an improvement over the prior art. That is not the case here. Beyond stating that the compounds are all steroids, no reason has been given as to why teachings related to one compound should be relevant to another. Although the compounds have a steroidal core, they contain other groups that are relevant to stability. One simply cannot make the leap that the examiner makes that all steroids are equal. (See for example *Brenner v Manson*, 148 USPQ 689 (S Ct 1966)).

Contrary to the examiner's view, this is not a situation where the applicant has simply discovered a new result. It is agreed that this is not patentable. The present invention requires a specific step, adjusting the pH to a defined value that is a new active step. There is therefore no analogy with *in re Kahn*.

It can be seen from the above that the amended claims are not obvious over the cited references, and meets the requirements of 35 USC 103.

It is therefore submitted that this application is in order for allowance and an early action to this end is respectfully solicited.

Respectfully submitted,



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